and conforms to the requirements prescribed therefor by specific regulations.

(d) Each sample submitted pursuant to the regulations in this chapter shall be addressed to the Commissioner. Its package shall be clearly identified as to its contents and shall bear the name and post-office address of the person submitting it.

(e) In addition to the information and samples specifically required to be submitted to the Commissioner by the regulations in this chapter, the person who requests certification of a batch shall submit such further information and samples as the Commissioner may require for the purpose of investigations to determine whether or not such batch complies with the requirements of §431.10 for the issuance of a certificate.

(f) Reference standards identical to working standards are available from: U.S.P. Reference Standards, 12601 Twinbrook Parkway, Rockville, Md. 20857, 301–881–0666.

[39 FR 18934, May 30, 1974, as amended at 41 FR 46852, Oct. 26, 1976; 43 FR 41195, 41197, Sept. 15, 1978; 45 FR 40111, June 30, 1980; 50 FR 7516, Feb. 22, 1985; 50 FR 8997, Mar. 6, 1985; 55 FR 11582, Mar. 29, 1990]

§431.5 Samples for sterility testing.

(a) *''Filling operation'' and ''sample'' defined.* (1) The term ''filling operation'' when used in connection with samples of a batch required for sterility testing refers to that period of time not longer than 24 consecutive hours during which a homogeneous quantity of drug is being filled continuously into market-size containers and during which no changes are made in the equipment used for filling. (Short rest periods for operators of the filling equipment and the time required to change operators between consecutive shifts are not considered as a break in continuity of the filling operation.) If more than one filling device is used during the filling operation, the samples shall include immediate containers filled by each device, and each such container shall be identified with a mark corresponding to that assigned to the filling device. If more than one filling operation is required to fill a batch, each container in the sample shall be identified with the number of the operation.

(2) For the purpose of sterility testing, the term ''sample'' means the total number of containers taken from each filling operation.

(b) *Packaging requirements for samples.* If a batch of a sterile antibiotic is packaged for repacking or for use as an ingredient in the manufacture of another drug, the sample required for sterility testing may be packaged in one container, in lieu of 20 containers, or in two containers in lieu of 40 containers, under the following conditions:

(1) The weight or volume of the sample is equivalent to the composite weight or volume required for a multiple container sample;

(2) The sample is a composite of samples taken from all parts of the batch; and

(3) The sterility test method prescribed for the drug by the regulations in this chapter is ''Bacterial membrane filter method'' described in §436.20(e)(1) of this chapter.

§431.10 Certification.

(a) If it appears to the Commissioner, after such investigation as he considers necessary, that:

(1) The information (including results of tests and assays) and samples required by or pursuant to the regulations in this chapter have been submitted, and the request for certification contains no untrue statement of a material fact; and

(2) The batch complies with the regulations in this chapter and conforms to the applicable standards of identity, strength, quality, and purity prescribed by the regulations in this chapter;

the Commissioner shall certify that such batch is safe and efficacious for use, subject to such conditions on the effectiveness of certificates as are prescribed by §431.11 and shall issue to the person who requested it a certificate to that effect.

(b) If the Commissioner determines, after such investigation as he considers to be necessary, that the information submitted pursuant to the regulations in this chapter, or the batch covered by such request, does not comply with the requirements set forth in paragraph (a)

of this section for the issuance of a certificate, the Commissioner shall refuse to certify such batch and shall give notice thereof to the person who requested certification, stating his reasons for refusal.

(c) All statements, samples, and other information and materials submitted in connection with a request for certification shall be considered to be part of such request.

(d) Compliance of a drug with the standards of identity, strength, quality, and purity prescribed by regulations in this chapter shall be determined by the tests and methods of assay prescribed for such drug by regulations issued under this chapter.

(e) The regulations in this chapter, prescribing tests and methods of assay for antibiotic and antibiotic-containing drugs, shall not be construed as preventing the Commissioner from using any other test or method of assay in his investigations to determine whether or not:

(1) A request for certification contains any untrue statement of a material fact; or

(2) A certification has been obtained through fraud, or through misrepresentation or concealment of a material fact.

(f) Except as specifically provided by the regulations in this chapter, no provision of any regulation shall be construed as exempting any certifiable antibiotic drug from any applicable provision of the act or any regulation thereunder.

§431.11 Conditions on the effectiveness of certificates.

(a) A certificate shall not become effective:

(1) If it is obtained through fraud or through misrepresentation or concealment of a material fact;

(2) With respect to any package unless it complies with the packaging requirements, if any, prescribed by the regulations in this chapter which were in effect on the date of the certificate;

(3) With respect to any package unless its label and labeling bear all words, statements, and other information required by the regulations in this chapter; or

(4) With respect to any package of a certifiable antibiotic drug subject to the regulations in this chapter, when it is included in a packaged combination with another drug, unless such other drug complies with the requirements of the regulations in this chapter.

(b) A certificate shall cease to be effective:

(1) With respect to any immediate container after the expiration date, if any, prescribed by the regulations in this chapter;

(2) With respect to any immediate container when it or its seal (if the regulations in this chapter require it to be sealed) is broken, or when its label or labeling is altered, multilated, destroyed, obliterated, or removed in whole or in part, or ceases to conform to any labeling requirement prescribed by the regulations in this chapter, except that:

(i) If the drug in such container is repacked or used as an ingredient in the manufacture of another drug, and certification of the batch thus made is requested, such certificate shall continue to be effective for a reasonable time to permit certification or destruction of such batch;

(ii) If the drug is in a container packaged for dispensing and is used in compounding a prescription issued by a practitioner licensed by law to administer such drug, such certificate shall continue to be effective for a reasonable time to permit the delivery of the drug compounded on such prescription; or

(iii) If its label or labeling is removed in whole or in part for the purpose of relabeling and supplemental certification of the relabeled drug is requested, as provided by §433.12 of this chapter.

(3) With respect to any immediate container of penicillin when it is included in the packaged combination penicillin with aluminum hydroxide gel or penicillin with a vasoconstrictor, or to any immediate container of bacitracin when it is included in the packaged combination bacitracin with a vasoconstrictor, except that when certification of the batch so included is requested, such certificate shall continue to be effective for a reasonable time to permit certification of such